DRUGS AND DEVICES ACTIONABLE BECAUSE OF POTENTIAL DANGER WHEN USED ACCORDING TO DIRECTIONS

3550. Action to enjoin and restrain violations of Sections 301 (a) and 301 (k) with respect to male and female hormones. U. S. v. El-O-Pathic Pharmacy, Martin A. Clemens, and Vita Pharmacals, Inc. Tried to the court. Judgment denying application for permanent injunction reversed upon appeal. (Inj. No. 216.)

COMPLAINT FILED: September 2, 1949, Southern District of California, against the El-O-Patic Pharmacy, a corporation, Hollywood, Calif., and Martin A. Clemens, manager. On September 20, 1949, the complaint was amended to include the Vita Pharmacals, Inc., Hollywood, Calif., as a defendant, and to charge Martin A. Clemens as manager of both corporations.

VIOLATION CHARGED: The complaint alleged that the defendants were distributors of certain *male and female hormones;* that the *male hormones* consisted of *methyltestosterone tablets* (10 milligrams and 25 milligrams), *methyltestosterone in linguet form* (5 milligrams and 10 milligrams), and *methyltestosterone combined with vitamin B_1 in linguet form;* and that the *female hormones* consisted of various preparations containing *alpha-estradiol* (ranging from .01 milligram to 0.5 milligram).

The complaint alleged also that the *male and female hormones* were manufactured outside the State of California and were shipped in interstate commerce to the defendants; that during the interstate journey, the drugs bore the legend "Caution: To be dispensed only by or on the prescription of a physician"; and that the defendants repacked and relabeled the drugs and sold and distributed them without a physician's prescription.

The complaint alleged further that the defendants were violating Section 301 (k) of the Act by causing the 5 milligram and 10 milligram *methyltestosterone linguets* to become misbranded while held for sale after shipment in interstate commerce, and that they were violating Section 301 (a) of the Act by causing the introduction into interstate commerce of misbranded 5 milligram and 10 milligram *methyltestosterone linguets* and *methyltestosterone combined with vitamin B_1 in linguet form.*

The above drugs were alleged to be misbranded under Section 502 (f) (1) in that the labeling of the drugs failed to bear adequate directions for use in all conditions for which they were prescribed, recommended, and suggested in the labeling and advertising matter disseminated and sponsored by the defendants, and under Section 502 (f) (2) in that the labeling of the drugs failed to bear adequate warnings against use in those pathological conditions where their use may be dangerous to health, in such manner and form, as are necessary for the protection of the user, since the technical medical terminology in which the labeling of the drugs was couched was inadequate to warn the ordinary lay users that use of the drugs may accelerate the malignant growth of cancer of the prostate gland or may cause sterility.

It was alleged also that the 5 milligram *methyltestosterone linquets* and the *methyltestosterone with vitamin B_1 linguets* were misbranded under Section 502 (a) in that the labeling of such drugs was false and misleading since the labeling represented and suggested that the recommended daily dosage was efficacious for use in the treatment of male hormone deficiency, whereas the recommended daily dosage would be entirely ineffective for such purpose; and that the 10 milligram *methyltestosterone linguets* were misbranded under Section 502 (j) in that such linguets were dangerous to health when used in the

dosage and with the frequency prescribed, recommended, and suggested in the labeling since such use of the linquets may result in sterility and may accelerate the malignant growth of cancer of the prostate gland.

With respect to the *methyltestosterone tablets* and the *alpha-estradiol* preparations it was alleged also that the defendants would likely cause the same violations of Sections 301 (a) and 301 (k) as they were causing with respect to the 10 milligram *methyltestosterone linquets* since the defendants had sold in the past such products freely without a physician's prescription and without adequate warnings; since the *methyltestosterone tablets* had the same dangerous potentialities as the linguets; and since the unrestricted use of the *alpha-estradiol* preparations by women may accelerate the malignant growth of cancer of the breast, cervix, and uterus, and may cause injury to the female generative system.

DISPOSITION: A temporary restraining order having been issued on September 2, 1949, the matter came on for hearing on the issuance of a preliminary injunction. The application for a preliminary injunction was denied on January 11, 1950, and on January 30, 1950, findings of fact and conclusions of law were filed to the effect that where the United States seeks a preliminary injunction to prevent alleged violations of the Federal Food, Drug, and Cosmetic Act, and it appears that an early trial can be had on the prayer for a permanent injunction which will substantially protect the public interest involved, a preliminary injunction should not issue.

On January 31, 1950, the case came on for trial before the court on the issue of granting a permanent injunction. For purposes of trial, the case against the Hudson Products Co., et al. (notices of judgment on drugs and devices, No. 3553) was consolidated with the instant case.

The evidence submitted at the trial of the consolidated cases consisted of a stipulated written record consisting of the pleadings and certain affidavits, together with a transcript of the criminal proceedings against the defendants in each of the consolidated cases which previously had been terminated. (See notices of judgment on drugs and devices, Nos. 2931, 2932.) The matter was taken under advisement by the court, and on May 22, 1950, after handing down findings of fact and conclusions of law, judgment was entered in each of the consolidated cases, denying the Government's application for a permanent injunction and dismissing the complaint for injunction.

An appeal was taken to the United States Court of Appeals for the Ninth Circuit, and on June 18, 1951, the following opinion was handed down by that court:

MCALLISTER, *Circuit Judge:* "This is an appeal from an order of the district court denying permanent injunctions in consolidated cases in which the government sought to restrain appellees from introducing certain allegedly misbranded drugs, known as hormones, into interstate commerce, and, further, to enjoin them from causing any acts to be done with respect to such drugs that would result in their being allegedly misbranded in (intrastate) commerce, in claimed violation of the Federal Food, Drug, and Cosmetic Act of 1938, as amended. Title 21 U. S. C. A., Sections 301 et seq.[1]

[1] 21 U. S. C. A., Section 331, provides as follows:
"Prohibited acts—
The following acts and the causing thereof are hereby prohibited:
(a) The introduction or delivery for introduction into interstate commerce of any food, drug, device, or cosmetic that is adulterated or misbranded.
* * *
(k) The alteration, mutilation, destruction, obliteration, or removal of the whole or any part of the labeling of, or the doing of any other act with respect to, a food, drug, device, or cosmetic, if such act is done while such article is held for sale (whether or not the

"The government's complaint asking for injunctions in the district court thus specified two types of prohibited acts which it alleged appellees violated; and the circumstances giving rise to such complaint are as follows: It appears that the hormones in question are manufactured by pharmaceutical corporations in the eastern part of the United States and shipped to appellees in California with labeling that states, in part, 'Caution: To be dispensed only by or on the prescription of a physician.' Thereafter, the appellees relabeled the drugs to eliminate this prescription statement; and the new labeling, it was claimed, caused the drugs to become misbranded within the meaning of the statute. 21 U. S. C. A., Section 352 (a), 352 (f) (1), 352 (f) (2), 352 (j). When appellees distributed these relabeled drugs in *interstate commerce*, it was alleged that they violated that section of the statute which prohibits the introduction of misbranded drugs into interstate commerce. 21 U. S. C. A., Section 331 (a); and when they distributed such relabeled drugs in *intrastate commerce*, it was claimed that they violated that section of the statute which prohibits the doing of acts with respect to the labeling of drugs while they are held for sale after shipment, if such acts result in the drugs being misbranded, 21 U. S. C. A., Section 331 (k).

"On appeal, the government contends that the hormones, introduced into interstate commerce, distributed, and sold by appellees, were misbranded, in violation of the statute, in that they did not bear adequate directions for use; that they were dangerous to health when taken as directed; and that they did not bear adequate warnings against use in those pathological conditions where their use might be dangerous to health; all in violation of the statute. Title 21 U. S. C. A., Section 352 (a), 352 (f) (1), 352 (f) (2), 352 (j).

"The district court held that the warnings on the cartons containing the drugs were sufficient in that they stated that the hormones were for use by adult males deficient in male hormone when small dosages are prescribed or recommended by a physician for palliative relief of such symptoms; that the maintenance dosage could be extended from three to six months under supervision of a physician; that before taking the hormone, a physician should be consulted, since the hormone would not aid or relieve symptoms not associated with male hormone deficiency; and that children and young adults must not use the hormone except under constant, direct supervision of a physician. Remarking that the government wanted the drugs in question to be sold only upon the prescription of a physician, the court concluded that the question as to what effects would follow from the administration of the drugs was in dispute; that the doctors could not agree on the subject; that the government had not sustained the burden of proof; and the court, accordingly, dismissed the case.

"It is the claim of the government that it has sustained the burden of proving that the hormones in this case are inherently dangerous; that they are not safe and efficacious for use except under the supervision of a physician; that they are not suitable for self-medication, since a layman could not know when they should be used and when they should not be used; that adequate directions for unsupervised lay use can not be written; and that such drugs, if sold legally

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first sale) after shipment in interstate commerce and results in such article being adulterated or misbranded."

21 U. S. C. A., Section 332, provides:

"Injunction proceedings—Jurisdiction of courts—

(a) The district courts of the United States and the United States courts of the Territories shall have jurisdiction for cause shown, and subject to the provisions of section 381 (relating to notice to opposite party) of Title 28, as amended, to restrain violations of section 331, except paragraphs (e), (f), (h), (i), and (j)."

21 U. S. C. A., Section 352, provides:

"Misbranded drugs and devices—

A drug shall be deemed to be misbranded—

(a) If its labeling is false or misleading in any particular.

* * *

(f) Unless its labeling bears (1) adequate directions for use; and (2) such adequate warnings against use in those pathological conditions or by children where its use may be dangerous to health, or against unsafe dosage or methods or duration of administration or application, in such manner and form, as are necessary for the protection of users: Provided, That where any requirement of clause (1) of this paragraph, as applied to any drug or device, is not necessary for the protection of the public health, the Administrator shall promulgate regulations exempting such drug or device from such requirement.

* * *

(j) If it is dangerous to health when used in the dosage, or with the frequency or duration prescribed, recommended, or suggested in the labeling thereof."

in interstate commerce, must be dispensed only upon prescription of a physician, in accordance with the regulations of the Federal Security Administrator.[2] The government further contends that the proofs disclose that the drugs in question failed to bear adequate directions for use, in that they are offered to the public as efficacious remedies for many conditions which are not mentioned in the labeling or directions for use.

"To these contentions, appellees reply that the statute in question is not susceptible of an interpretation that the Administrator, provided for therein, is empowered to determine what drugs may be sold only on prescription; that the labeling of appellees' drugs bears adequate directions for use and warnings within the meaning of the statute; that the drugs are not dangerous to health, within the meaning of the statute; that the findings of the district court are sustained by substantial evidence; and that, since they are not clearly erroneous, they must be accepted on appeal, and the judgment affirmed. Rule 52 (a), Federal Rules of Civil Procedure.

"The evidence in the district court consisted of a stipulated written record. It comprised the pleadings, affidavits, and a transcript of proceedings in the trial of a criminal case in which appellees were found guilty by the district court, sitting without a jury, of the offense of distributing misbranded male and female sex hormone drugs. The convictions were, essentially, based upon the conclusions and findings of the district court that the hormones were dangerous to health and that the labeling claims which appellees therein made for their hormones were false and misleading. The district court stated, in the criminal case, that it was convinced beyond a reasonable doubt, that indiscriminate distribution or dispensation for use of the hormones carried not only a potential but an actual danger of injury to some persons; that the leaflets and circulars enclosed in the packages by which deliveries of sales were made, were designed to create a belief that many persons were deficient in their natural testosterone, and that, by supplementing it with the drug called by various names, a synthetic testosterone, much benefit could be derived by the user; and that the court was convinced from the evidence that these drugs did not, other than within a restricted class of cases, produce many or any of the alleviatory and beneficial effects that the labeling given them by the defendants indicated, and encouraged readers to belive they would generally produce. Appellees did not file appeals in the criminal case, but paid the fines imposed upon them.

"After the convictions in the criminal case, a different judge was assigned to try the injunction cases now before us. The evidence in these consolidated cases, here on review, consisted of the record in the prior criminal case. No additional witnesses were produced and no oral testimony was submitted. While giving due consideration to the trial court's findings, to which they are justly entitled, and with reluctance to reverse them unless well persuaded, nevertheless, under such circumstances, they do not have the weight we would otherwise be obliged to concede to them, and the scope of review is *de nova;* for this court is in as good a position as the trial court was to appraise the evidence. Equitable Life Assur. Soc. of the United States v. Irelan, 123 F. 2d 462 (C. A. 9). See Stork Restaurant, Inc. v. Sahati, et al., 166 F. 2d 348 (C. A. 9); Murphey, et al. v. United States, 179 F. 2d 743 (C. A. 9); Orvis v. Higgins, 180 F. 2d 537 (C. A. 2); Blackner, et al. v. McDermott, 176 F. 2d 498 (C. A. 10); and while, under Rule 52 (a) of the Federal Rules of Civil Procedure, findings of fact in actions tried without a jury may not be set aside unless clearly erroneous, nevertheless a finding is 'clearly erroneous' when, although there is evidence to support it, the reviewing court, on the entire evidence, is left with the definite and firm conviction that a mistake has been committed; United States v. U. S. Gypsum Co., et al., 333 U. S. 364, 394.

"For an understanding of the issues involved, an outline of the nature, use, and effect of hormones, as disclosed by the evidence, may be helpful.

"The drugs here involved are male and female sex hormones. A hormone is medically defined as a chemical substance originating in an organ, gland, or part of the body, which is conveyed through the blood to another part of the body, stimulating it to increased functional activity, and increased secretion.

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[2] Title 21, Code of Federal Regulations, Sections 1, et seq. (1949 Ed.).

"The principal drug in question is testosterone, which is a male sex hormone. This hormone is generated by the reproductive organs of the normal adult male. Male sex hormones are also known as androgens, and female sex hormones, as estrogens. They are not only generated in the reproductive organs; the hormones, in this case, are prepared from extracts of animal tissues and fluids, as well as made synthetically by complex chemical fusions that have the qualities of natural hormones.

"Leaders of the medical profession in America, practitioners, professors of medicine, as well as research scholars, scientific men of conservative attitude, appearing as witnesses for the government in this case, referred to the 'dramatic results' produced by testosterone, and described the effects of its use as 'spectacular,' 'amazing,' 'astounding,' and 'absolutely wonderful.' But as government counsel observe, the drug is capable of dramatic good and, at the same time is capable of dramatic evil.

"The good and evil effects of the administration of testosterone are more readily appreciated when it is understood how the body naturally produces and utilizes this hormone. The natural generation of testosterone in the reproductive organs of the normal adult male is governed by a delicate endocrine, or glandular balance, that exists between such organs and the pituitary gland, the small gland located at the base of the brain, of which one function is the production of hormones known as gonadotrophins. These gonadotrophins stimulate the testes to produce spermatozoa and testosterone. Testosterone is responsible for the changes which characterize a boy's development through puberty to manhood. It causes an unfolding of the secondary sex characteristics such as growth of sex organs, muscles, enlargement of the larynx with consequent change of voice, and like developments.

"In the normal functioning of the pituitary and testicular glands, there is an interplay between the testicular hormone, testosterone and the pituitary hormones, gonadotrophins. If the production of the pituitary hormone decreases, the testes are no longer properly stimulated, and, as a result, they produce a lesser amount of testosterone and spermatozoa. The lowered body level of testosterone, in turn, stimulates the pituitary gland into greater activity. As described by one of the medical experts, its action is like a thermostat, as, when the heat drops, the thermometer records it and turns the furnace on. As the testosterone level drops, the pituitary gland is turned on to produce more gonadotrophins. However, if the level of the testosterone gets too high, then the activity of the pituitary gland is lessened, just as when the temperature gets too high, the furnace is turned off.

"With respect to the effect of the administration of sex hormones on human beings, the government's case rested on the testimony of witnesses who, from the evidence, appear to be among the foremost medical authorities in this country on the subject, comprising research specialists in hormones, heads of urology departments in great hospitals, professors of urology, research urologists, professors of pharmacology and toxicology, professors of surgery, specialists in the study and treatment of cancer, professors of anatomy, and endocrinologists, as well as medical practitioners in these various fields of medicine.

"Among these witnesses was Dr. Charles Huggins, Professor of Urology and head of that department in the hospital of the University of Chicago, whose work, for twelve years prior to the trial was devoted almost exclusively to the male hormone, and its action in normal and cancerous individuals, and who, from the evidence, is apparently the chief authority on the effects of testosterone. According to Dr. Huggins, the administration of this drug results in startling changes in men, known as hypogonads, and in castrates. Describing a hypogonad as a man in whom the male sex hormone is produced in small amounts or not at all, Dr. Huggins testified that it is usually—not always—a congenital state in which the reproductive organs and secondary sex characteristics remain undeveloped; the male speaks with a soprano voice; he has no growth of hair on the face or the body; and is completely unable to have any sex relationship. By administering male hormones to such a person, his sexual 'drive' is restored, as well as the normal male sex characteristics. Impotence is replaced by potency. 'In hypogonadism, it had spectacular effects.' If testosterone is administered to castrates, most of whom have suffered such impairment as a result of the explosion of land mines during the war, it will develop or restore their sex drive and secondary sex characteristics, and make such persons practically normal males. Among

methods to ascertain whether a person suffers from hormone deficiency, are clinical observations and complex laboratory tests.

"Dr. Norris J. Heckel, Professor of Urology at the College of Medicine of the University of Illinois, and Chairman of the Department of Urology at the Presbyterian Hospital in Chicago, a leading medical authority on this subject, testified that when, by the action of testosterone, 'you can take a female male and make that individual into a man and establish him back into his community and make him a perfectly normal male, it is really amazing and astounding.'

"The administration of testosterone is, however, accompanied by grave dangers to the health, and, often, to the life of the person to whom it is administered. Dr. Huggins testified that the administration of testosterone to a child would result in tremendous growth of the sex organs and bring about the secondary sex characteristics of change and depth of the voice and growth of hair on the face and chest; that to give the drug to a child of five or ten years of age would result in a tremendous sex drive; that it would render a child sexually mature at the age of two years with the exception that sperms would not be produced.

"According to the evidence of the government medical expert witnesses, it appears that, from experimental research studies conducted by them, the administration of testosterone inhibits or reduces the activity of the pituitary gland in the production of gonadotrophins, and this, in turn, results in a decrease in the activity of the testes, both in the production of spermatozoa and in the production of testosterone. As a consequence, the administration of testosterone, by upsetting the hormonal balance of the body, tends to produce a condition of infertility or sterility that may continue for months or years, depending upon the amount and duration of administration, and the condition of the reproductive organs. Moreover, on the basis of research, it appears that men, from the age of forty to sixty, are more likely to be susceptible to the damaging effects of testosterone than younger men.

"The great dangers, however, encountered in the administration of testosterone appear, from the evidence, to be concerned with the activation and acceleration of unperceived, dormant, or inactive cancer growths in the human body. A man may have cancer of the prostate gland and not be aware of it, for there are no symptoms through which a person may diagnose his own case; but this type of cancer is the cause of death of 5 per cent of men over fifty years of age. From post-mortem examinations, it appears that between one-sixth and one-third of men over fifty years of age have dormant lilliputian cancers of their prostate glands. Diagnosable cancer of the prostate ranges from one out of thirty-five men aged fifty who consult with a urologist with regard to difficulty in urinating, to one out of twelve aged sixty, with the same difficulty. Prostatic cancer is usually diagnosed by a physician by rectal examination, with palpation of the prostate gland; and various laboratory tests, including biopsy, or microscopic examination of small samples of testicular tissue removed by surgical operation, are also available. Early prostate cancer is successfully treated by the removal of the entire prostate gland.

"The remarkable relationship of cancer to testosterone is perceived when testosterone is administered to a man who has a dormant or inactive cancer of the prostate gland. The drug will activate such cancers and greatly accelerate its growth, causing it to metastasize, or spread, to other parts of the body, eventually becoming impossible to control; and even testosterone produced naturally by the body tends to activate such dormant cancers. However, although dormant or active cancer of the prostate gland occurs most frequently in middle-aged or older men, nature itself provides a mechanism whereby the body's production of testosterone is reduced as much as 50% in those age groups. Consequently, while a large number of men over fifty years of age have dormant cancerous cells in their prostate glands, the lowered natural supply of testosterone usually permits those cells to remain dormant and harmless. Yet they can be activated and stimulated into malignant cancers by the artificial administration of testosterone.

"Where cancer has spread beyond the confines of the prostate gland, treatment calls for the elimination of testosterone from the body as far as possible. This is sometimes accomplished by surgical castration, which removes the major source of the body's supply of testosterone. It has been found that

while the administration of testosterone has made prostatic cancers flourish, the removal of testosterone causes such cancers to wither, shrink, and disappear.

"During the last ten or twelve years, another remarkable discovery has been made in this medical field. It has been found that the administration to a man suffering from cancer, of estrogenic drugs, or female hormones, causes the cancer to decrease. Even where the cancer has spread to a man's chest, which has been riddled with metastatic lesions, the administration of female hormones—which are antagonistic to male hormones and neutralize them—has caused such lesions to shrivel up in an amazing way, and disappear. While it appears that the administration of female hormones to a man suffering from cancer may cause such cancer to dry up and disappear, the administration of female hormones to a woman suffering from cancer—before her change of life—accelerates its growth; and, it is to be remarked, many women who have, for instance, cancer of the breast, are not aware of that fact without medical observation and diagnosis. Female hormones accelerate malignant growth not only of cancer of the breast, but of the uterus, to the point where its control becomes impossible. Yet when male hormones have been administered to women suffering from such cancers, they have decreased.[3]

"High potency female sex hormones, which are administered orally, by injection, or by rubbing on the skin, are useful in breast development in limited cases of young women, usually under twenty, who manifest hormone deficiency, in terms of ovarian function, with the result that the breast and genital tracts are undeveloped; but there is no direct relationship between female sex deficiency and small breasts. A woman may have small breasts, yet not suffer from a hormone deficiency; and if she does not suffer from such deficiency, the use of hormones will be of no value in causing breast enlargement. There are no subjective symptoms by which a woman can correctly diagnose herself as having a female sex hormone deficiency.

"According to the evidence of the government's expert medical witnesses, the administration of testosterone is contra-indicated, or medically forbidden, in all cases where cancer is suspected in men, and, likewise, female hormones, in the presence of cancer in women, at or past the menopause, although in older women, with seeming incongruity, they sometimes inhibit such growths.

"Male hormones, aside from their use in treating cancers in women, are properly prescribed, according to the government medical witnesses, with some minor exceptions,[4] when there is no suspicion of cancer,[5] and only in the rare

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[3] It is interesting to note that for the first time in medical history, cancer of the thyroid gland in the neck has responded to treatment with male hormone, in the case of a woman who had been ill with such cancer for nine years, and who, since the hormone treatment, left her bed, and has since been leading a normal life for the past eight months, according to the report of Dr. Henry M. Lemon, of Boston University, to the American Cancer Society. "The patient's bones still are shot through with cancer," Dr. Lemon stated. "There is no telling whether any of this can be cleared up and, if so, how long the remission will last." Large doses of X-ray had previously been tried without success. The cancer did not pick up radio-active iodine, as some thyroid cancers do, so that treatment offered no hope. Scientific interest in this case, Dr. Lemon pointed out, centers on the opportunity to study just what effect the male hormone has on protein synthesis in thyroid cancer. Science News Letter, March 31, 1951.

[4] It has been found that testosterone produces good results in causing growth of epithelium where the kidneys are damaged by nephritis; that it has been noticed that the drug brings about re-growth of tissue, in the healing of indolent ulcers of the lower leg that have failed to heal by the use of any other method; and that, in cases where elderly men wake up in the night, become disoriented and mentally disturbed, testosterone is sometimes used with good effect to remedy such a condition.

[5] At the Annual Meeting of the American Medical Association, held on June 12, 1951, Dr. Huggins is stated to have reported additional discoveries with reference to the relationship between hormones and cancer, according to a signed article by William L. Laurence, noted science news reporter of the New York Times. The report, according to Mr. Laurence, announced that two human patients who were near death from a recurrence of cancer of the prostate gland, "have gained a new lease on life" after total removal of both their adrenal glands. "The removal of both adrenal glands, ordinarily essential to the maintenance of life, has been made possible by the availability of cortisone, one of the vital life-giving hormones secreted by the outer layer of the glands, which are located astride the kidneys.

"The new surgical procedure, a major development in the art of surgery, was described before a large audience of distinguished physicians and surgeons from all parts of the country by Prof. Charles B. Huggins and Assistant Prof. D. M. Bergenstal of the School of Medicine, University of Chicago.

"Professor Huggins gained international renown about twelve years ago when he discovered that prostate cancer thrives on the male hormones and that castration, which eliminates the secretion of male hormones, shrinks and checks its further growth. As a

instances where the patient is suffering from a male hormone deficiency—that is, where he is a castrate, or a hypogonad; and only between one to two men out of a thousand who are admitted for hospital treatment are hypogonads. Dr. Huggins testified that only about thirty men in the last eleven years have been treated, at his hospital, for male hormone deficiency. Female hormones, aside from their use in treating cancers in men, are properly prescribed only where there is no suspicion of cancer and where the patient is suffering from the effects of a female hormone deficiency.

"Among the witnesses for the government was Dr. Elmer Belt, urologist, associated with research work in the Belt Urological Group, and a member of the California State Board of Health, who had observed more than 1,000 cases of prostate cancer in men; Dr. Ian Macdonald, Associate Professor of Surgery at the University of Southern California School of Medicine, who had treated more than 1,000 cancers in women; as well as others who are among the pioneers and most experienced leaders in the field of hormone research, and in the use of such drugs in cases of hormone deficiency and cancer. In addition to the evidence above outlined to the effect that sex hormones are dangerous and highly potent, but drugs which are useful in certain cases, it appeared, according to the government witnesses, that the consensus of informed and expert opinion was that the dosages of testosterone suggested by appellees' labeling of the drugs would accelerate the growth of a dormant or active cancer of the prostate gland; that no lay person was capable of judging whether he should use such drugs; that they might result in the greatest danger to his health and life; that the judgment as to who should receive and who should not receive the drugs was a matter for doctors alone and a consideration of the highest importance to the patient; that the drug should always be administered under the supervision of someone with knowledge of the matter; that to use the hormones required the most meticulous diagnosis and supervision, and that it is necessary to maintain such supervision over the patient during the course of the treatment, controlled by frequent examinations; and that, as one of the government experts said, in referring to the drug, 'The amount of potential harm it has is much greater than the good it can do, if used unbridled.'

"Appellees introduced as expert testimony with reference to the use of the drug, the evidence of three practicing physicians. However, none of these witnesses was a urologist, research expert, or cancer specialist, and none had ever conducted any clinical, laboratory, or scientific tests with regard to hormones or cancer. One of the witnesses, during his ten years of general practice, had seen cancer of the prostate gland about once a year; and although he gave thousands of physical examinations during the war, he stated that he found no such cancers except on very rare occasions. When a patient calls upon him complaining of unusual weakness, loss of memory, inability to concentrate, nervousness, or general fatigue, or a combination of these complaints, he talks with him a few moments to try to determine if there is anything else that bothers him, such as a bad heart; and if he can determine that the patient has no organic, pathological condition, he prescribes or injects male hormones.

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result, many thousands of human beings, who otherwise would have been doomed to certain death, are still alive, many of them as long as twelve years after operation.

"Castration is accomplished either by surgery or by the administration of female hormones that neutralize the male hormones.

"Unfortunately many of the prostate cancers recur after either surgical or chemical castration, and in such cases there has been until now nothing that medicine or surgery could offer to these victims. The reason for such recurrences is that the adrenal glands also secrete large quantities of male hormones, and that after castration by either method they are stimulated to increase their output.

"However, there was nothing that could be done for these unfortunates since it was impossible to remove the adrenal glands because the adrenal hormone cortin is vital for the maintenance of life. The availability of cortisone, which is widely used in the relief of the symptoms of rheumatoid arthritis, rheumatic fever and many other major chronic ills, has at last opened the way for adding further years to the lives of prostate cancer victims.

"As little as twenty-five to fifty milligrams of cortisone taken daily by mouth, Professor Huggins reported, has maintained the patients whose adrenals have been removed, in good health three and four months, respectively, after operation. Both of them have gone back to work.

"While the new surgical procedure is still in its exploratory stages, it offers new hope for thousands of victims of prostate cancer, of whom more than 2,000 die every year. It also opens a new surgical approach to high blood pressure, in which the adrenal glands appear to be somehow involved, and lends further support to the hypothesis that cancer in general is the result of an imbalance in glandular secretions." New York Times, June 13, 1951.

He takes no tests of the patient, and prescribes testosterone to patients on an average of about once a day. He further stated that he has never encountered what he considers adverse results but has occasionally had good results, many of his patients being relieved of the symptoms above mentioned. He further stated that his reading on the subject suggested that testosterone aggravates or might possibly aggravate cancer of the prostate, but that the literature on the subject is not uniform, there being much confusion. He himself has no opinion on the subject. Many doctors do not know, and he stated that he is one of them. He doubts that the administration of the drug produces sterility. However, he does not believe he would prescribe the drug to a man who wished to procreate, or to a patient in whom he found any suggestion of cancer of the prostate.

"Another of appellees' medical witnesses testified that he frequently prescribed the drug. If a man in middle life comes to him and complains of nervousness, flushes, sweats, chills, general weakness, lack of physical strength, impaired memory, inability to concentrate on activities, and a tendency to evade them, he takes a general history of the person and his past illnesses, and after a complete physical examination, if he finds no evidence of a disease of a specific nature, he prescribes or administers testosterone. He has done this on many occasions and found, as a result, the patient's symptoms appeared relieved. He stated that on no such occasion has he ever encountered adverse results. He associates the 'male climacteric' with a diminution of the secretion of the interstitial cells of the testes. He prescribes the drug about once a week. In his practice of thirty years, he has seen three cases of cancer of the prostate. If a patient evinces some suspicion of prostatic cancer, he refers him to a urologist. He would, however, prescribe female hormones to a woman suffering from cancer if he thought she needed it; and he stated he would also prescribe testosterone to a man with cancer of the prostate if, in his opinion, he needed it, his determination in such a case depending on whether the patient had the 'middle-aged symptoms.' While he considered one of the government experts on the subject an eminent physician in his field, he declared that he would 'never accept any medical man as an authority anywhere.'

"The third medical witness for appellees was a physician of high scholastic attainments during his college work, who had been attached to the Veterans' Administration for two years after the completion of his medical studies, and had been in general practice one year at the time of his testimony. He associates the 'male climacteric' with a hormone deficiency, the symptoms being a loss of libido, or sexual drive, loss of a sense of well-being, nervousness, irritability, and sleeplessness. When men of middle age complain of these symptoms, he prescribes testosterone, and the patient thereafter often appears definitely relieved. He tries the drug out on such patients, and if it helps them, concludes that they suffer from a hormone deficiency. Prior to prescribing the drug, he gives a general physical examination, but does not give the various tests mentioned by the government medical witnesses, as the general practitioner does not have the equipment to do so, and the patient doesn't have the funds to pay for such tests. He stated that he had read the literature relating to testosterone and its relationship to cancer of the prostate, but that the articles are pro and contra. Based on what he has read and on his experience, he firmly believes that testosterone is not dangerous. It may be, incidentally, said that the opinion of the government expert witnesses in this field is that a condition, described by appellees' witnesses, as the 'male climacteric,' or a male change of life, does not exist, although some of the government's witnesses referred to a certain 'unusual and rarely encountered condition' of hormonal deficiency, as a male climacteric. But, according to the government's witnesses, there is no relation between middle age and a condition of hormone deficiency.

"Much of the testimony of appellees' medical witnesses—in fact, the whole force of the testimony of two of the three witnesses, who are of the opinion that testosterone has no effect upon male fertility, and who see no danger in its administration to patients suffering from cancer—makes most incongruous appellees' insistent claims in this case that the labels attached to the drugs they distribute adequately warn against the danger of using the drug by anyone who suffers from cancer of the prostate, and caution against its use

for the reason that it may result in infertility.[6] Moreover, the same testimony of appellees' medical witnesses was considered in the criminal cases, and was there rejected by the court which found that the drugs were dangerous; that appellees had made representations designed to create a belief that most persons were deficient in their natural testosterone, and that by supplementing it with synthetic testosterone, much benefit would be derived; and finally, that the court was convinced that such drugs, other than within a restricted class of cases, did not produce any of the alleviatory and beneficial effects that the label given them by appellees indicated and encouraged prospective buyers to believe they would produce. Having been convicted in those cases, having paid their fines without appeal, and having purportedly attempted to remedy the labeling complained of in order to comply with the law as there adjudicated, it may be supposed that appellees accepted the court's findings in the criminal cases as valid. If such findings were valid, accepted, and unchallenged in the criminal cases, they would seem equally valid in the instant case in so far as here applicable, since they would rest upon the same proofs and evidence in both cases. In fact, a puzzling aspect of the arguments of appellees in this case is that they are not, in this instance, challenging the dangerous potentiality of the hormones. Having accepted their conviction in the criminal cases as valid, they here contend that the changes in their labeling have brought their drugs into full compliance with the law.

"With reference to appellees' arguments that the credibility of two of the important government medical witnesses had been conclusively impeached, it appears that one of the appellees, and others employed by them, called on the physicians in question, requesting a prescription of testosterone. In one of the cases, it was represented that appellee's doctor, in another state, whose name he gave, had prescribed the drug regularly; that his doctor had told him to call upon the witness in case of need; and that, at the time, he required a further supply of the drug in order to continue the prescribed treatment. In another case, a prescription label on a bottle was shown to the doctor, indicating that the drug had been prescribed by a physician in another state, and the witness was asked to prescribe the drug in order to continue the treatment, which, it was represented, had been theretofore beneficial. Another instance was similar to the foregoing. We are not impressed with these contentions that, because the drug was prescribed by the government witnesses under such circumstances, the credibility of the witnesses was impeached in any important particular.

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[6] Typical label:

(Front Panel)

"VITA HORMONES 100 Tablets

Each Tablet Contains 10 Mg Methyl Testosterone.

SUGGESTED DOSAGE: One tablet upon arising before breakfast or one tablet shortly before retiring. Tablets should be held between gum and cheek, or under tongue, and allowed to dissolve slowly, so that hormone is absorbed by mouth tissues (saliva may be swallowed while tablet is in mouth, but do not swallow tablet). The maintenance dosage can be extended from three to six months, under supervision of a physician.

DIRECTIONS: For use by adult males deficient in male hormone when small dosages of male hormone are prescribed or recommended by a physician for palliative relief of such symptoms.

Distributed by VITA PHARMACALS, INC.
1109½ No. Western Ave. Hollywood 27, Calif.
HOllywood 9–1722

(Read Side Panels)

(Side Panel)

"It is impossible for a layman to determine whether he has a male hormone deficiency, as similar symptoms may be caused by other conditions. Therefore, before taking testosterone a physician should be consulted, since testosterone will not aid or relieve symptoms not associated with male hormone deficiency. Children and young adults must not use except under constant direct supervision of a physician.

(Side Panel)

"CAUTION: The male hormone should not be taken by anyone with carcinoma of the prostate or urinary retention probably due to carcinoma of the prostate or by anyone with cardiovascular disease, defects of spermatogenesis, sterility whether absolute or partial, or debilitation due to disease. Caution should be exercised when taking hormones for long periods since they have been reported as inhibiting spermatogenesis. Take only as directed."

"In this controversy, it is, of course, not to be supposed that this court assumes to act as an arbiter between conflicting medical opinions or schools of scientific thought. We have to determine the case solely on the evidence before us and the law. From the evidence before us, we are of the opinion that, while there is some difference of view, the expert testimony of the government's medical witnesses in this case is entitled to far greater weight than the testimony of other witnesses. We are not bound to reject informed medical judgment every time medical witnesses can be produced who blindly adhere to a curative technique discredited by reliable scientific experiences. See Reilly v. Pinkus, 338 U. S. 269. The testimony of the government's witnesses here appears to us completely credible and persuasive, and we accept it, in so far as this case is concerned, as proof of the facts in controversy. From such evidence, we are of the opinion that the drugs in question are inherently dangerous; that they are not safe and efficacious for use except under the supervision of a physician; and that they are not suitable for self-medication, since a layman can not know when they should be used and when they should not be used. Moreover, it is to be remarked that appellees' labels themselves, set forth that it is impossible for a layman to determine whether he has a male hormone deficiency; that before taking testosterone, a physician should be consulted; that children or young adults must not use the drug except under constant direct supervision of a physician; that it should not be taken by anyone with cancer of the prostate, or defects of spermatogenesis; and that it is for use by adult males deficient in male hormone, when small dosages are prescribed or recommended by a physician. These labels themselves clearly demonstrate that adequate directions for unsupervised use can not be written; and the testimony of the government's medical witnesses, which we accept, only strikingly emphasizes this important and crucial fact. Obviously, in such cases, the direction on the label that 'a physician should be consulted,' and the directions that the drug be used when dosages are prescribed or recommended by a physician, are not enough to constitute 'adequate directions for use' within the meaning of the statute.

"Since the drugs in question are inherently dangerous and not safe and efficacious for use except under the supervision of a physician, in view of the fact that a layman would not know when and when not to use them, and since adequate directions for unsupervised lay use can not be written, such drugs, if sold legally in interstate channels, can only be dispensed if the label bears, in accordance with the statute, 'adequate directions for use,' in the light of the given circumstances. The only adequate instructions for use in such cases would seem to be a caution that it be used only on the prescription of a physician. Would such a caution or such a direction constitute 'adequate directions for use' within the meaning of the statute? The inscription on a label, 'Caution—To be used only by or on the prescription of a physician,' would appear to constitute what is comprised within 'adequate directions for use' acording to the intendment of the law. United States v. Sullivan, 332 U. S. 689, 691. It is to be, of course, observed that the Supreme Court, in the above case, remarked that such an inscription appeared to constitute adequate directions, *since it was required by the regulation issued by the Administrator pursuant to authority of the Act.* And in this regard, we are mindful of the strenuous argument addressed to the court by counsel for appellee to the effect that the only power which the statute confers upon the Administrator to issue regulations in such cases, is authority to issue regulations exempting drugs from the requirement of 'adequate directions for use,' when that requirement is not 'necessary to the protection of the public health'; and that, accordingly, the statute gives the Administrator no power to issue regulations providing that drugs be sold only on the prescription of a physician.

"Necessarily, therefore, counsel for appellees finds his argument in conflict with the above statement of the Supreme Court in the *Sullivan* case, since he contends that when the Administrator exempts a drug from such directions, he has no authority to do anything more, such as, in this case, requiring, by regulation, compliance with other conditions and safeguards which, in his discretion, seem proper and necessary for the protection of the public health. The statute, however, does not state the exemption. It authorizes the formulation of the exemption by regulations. See Arner Co. v. United States, 142 F. 2d 730, 736 (C. A. 1). The statute provides that, if the requirement of

adequate directions is not necessary to the public health, the Administrator is empowered to promulgate regulations exempting the drug from such requirement. The government takes the stand that the Administrator may exempt the drug from the requirement of adequate directions for use, as not necessary to the public health, *provided* that there be compliance with the regulation requiring the label to state that the drug be used only on the prescription of a physician. Unless contrary to law, arbitrary, or unreasonable, the terms of exemption from adequate directions for use can be prescribed, in the discretion of the Administrator. Arner Co. v. United States, supra.

"May the Act be construed to authorize such exemption, conditioned upon compliance with the requirement that the drug be used only on the prescription of a physician? The statute is remedial and should be liberally construed so as to carry out its beneficent purposes, Research Laboratories v. United States, 167 F. 2d 410 (C. C. A. 9); and its construction should be infused by regard for such purposes, touching phases of the lives and health of people which are largely beyond self-protection, Arner Co. v. United States, supra. The Act as a whole was designed primarily to protect consumers from dangerous products, United States v. Sullivan, supra; its purpose is to protect the public, the vast multitude which includes the ignorant, the unthinking, and the credulous who, when making a purchase, do not stop to analyze. United States v. 62 Packages of Marmola Prescription Tablets, 48 F. Supp. 878, Aff. 142 F. 2d 107 (C. A. 7). See also Pasadena Research Laboratories v. United States, 169 F. 2d 375 (C. A. 9).

"A liberal interpretation of the Act, having in mind its background and purposes, requires us to sustain the action of the Administrator on the ground that he was empowered, under the statute, to exempt by regulation the drugs in question from the requirement that the label bear adequate instructions for use, conditioned upon its bearing an inscription that it be used only on the prescription of a physician. Under such construction, the regulation is not contrary to law, arbitrary, or unreasonable. This is not the same as conferring upon the Administrator a general authority to create classes of drugs or to specify the manner in which drugs of each class are sold, as argued by appellees; but where no adequate directions for use of specified dangerous drugs can be written for purposes of self-medication by a layman, and they can be safely taken only upon the advice and under the supervision of a physician, it is within the statutory power conferred upon the Administrator to require, by regulation, that the label set forth that they be taken only upon prescription of a physician. From another viewpoint, it would seem, from the evidence, that, aside from the regulation, the only adequate direction for use of the drug in question would be a requirement that it be taken only on the prescription of a physician and that, in default of a label embodying such direction, the drug would be misbranded under the statute. 21 U. S. C. A., Section 352 (f) (1). It is our conclusion and judgment that appellees' drugs did not bear adequate directions for use, and must, therefore, be deemed to be misbranded.

"Were it necessary to decide this case on certain additional grounds relied on by the government, we would find ourselves in agreement with its conclusions therein. The government contends that, from another aspect, the labeling of appellees' drugs fails to bear adequate directions for use, because it does not state the ailments of the body for which the drug is, through any means, held out to the public as an efficacious remedy. The evidence discloses that prior to the trial of the criminal cases, appellees' labeling and circulars stated that 'lack of sexual power' and 'lack of sexual desire' were remedied by testosterone; that it restored 'sexual desire and ability to fulfil it'; and that 'the male hormone discloses magic far beyond the merely sexual.' Shortly after the criminal convictions on July 13, 1949, appellees advertised in newspapers: 'Sensational New Formula! Male Hormones. Testosterone now combined with Vitamin B at a new low price. Mailed to you in plain wrapper. Send check, cash or money order. CAUTION! Take only as directed. DOUBLE YOUR MONEY BACK GUARANTEE. If, after taking these tablets for at least 10 days, you don't feel that you are deriving benefit from their use, return box and the unused tablets and we will cheerfully give you DOUBLE your money back.' Another newspaper advertisement set forth: 'Men Over 40. The New Hormone Tablets. Testosterone

Propionate. Full potency' with a guarantee of money refunded if the purchaser was not benefited within ten days. In addition, shortly after the criminal convictions, appellees sent out circulars to druggists stating: 'Dear Sir: Everybody's talking about hormones . . . hormones mean big volume and new profits to all druggists . . . hormones are the hottest thing in pharmaceuticals today . . . they'll soon be bigger than vitamins everywhere. There's been a flood of publicity, a best-selling book, dozens of national magazine articles, countless newspaper stories.' One circular sent to individuals through the mail gave a bargain price list of male hormones in lots up to 1,000 tablets, regular strength, and 500 tablets, double strength, with the statement: 'Take only as directed.' One of the circulars to druggists announced:

> Thousands of men and women everywhere are interested in hormones—need hormones—want hormones. They'll buy them wherever they can get them.
>
> Most people don't know where to get them!
>
> That's why Hudson Products Co., Inc., is launching an intensive national advertising campaign, telling every man and woman they can buy Hudson Hormones at their favorite drugstore. Twenty-five million match books will be circulated in California alone.

Moreover, it appears that almost immediately after the criminal convictions, appellees bought up extensive lists of persons who had previously purchased male hormones when they were sold under the widespread advertising and representations condemned, in effect, in the criminal cases, in order to circularize such persons and keep them as customers.

"It is difficult to discern any legitimate purpose in an intensive advertising campaign to tell every man and every woman that they can buy these dangerous drugs at their favorite drugstore, if they are to be taken only in consultation with a physician and when prescribed or recommended by him. In the light of these circulars and advertisements, it is impossible to conclude that the drugs were being sold for the limited purpose, set forth in the directions for use—to be taken, as the label stated, after consultation with a physician; and for use by adult males deficient in sex hormones, 'when small dosages of male hormone are prescribed or recommended by a physician' for palliative relief of such symptoms.

"The district court, in the criminal cases, had found that the indiscriminate distribution or dispensation of testosterone carried not only a potential but an actual danger of injury, and that, outside a restricted class of cases, the drugs produced none of the benefits which appellees encouraged the readers to believe they would produce. If appellees accept this finding, as they claim they do, then, for what purpose are they now distributing this dangerous drug in such an indiscriminate way and in such huge quantities? It is plain they are selling it for uses other than set forth in the directions in the labels. Twenty-five million match cover advertisements for distribution in California alone is hardly assurance that appellees are limiting the sales of these dangerous drugs to such restricted legitimate use as was mentioned by the district court in its findings in the criminal cases, or established by the evidence in this case. It is impossible to reconcile appellees' claimed acceptance of the court's conclusions in the criminal cases and their contention that they have since brought their labeling in full compliance with the law therein set forth, with their conduct since that time. The conclusion is inescapable that appellees are capitalizing on their previous representations and advertisements, and that the drugs are still being sold indiscriminately for 'overcoming impotence,' 'lack of sexual power,' and the like, that brought about their convictions in the criminal cases, although this is largely implicit rather than explicit in their labeling, advertising, and mail order business. Yet, this was not wholly implicit, for circulars distributed with other circulars relating to hormones at bargain prices, advertising a drug for certain sexual purposes; statements in circulars distributed in mail order letters that 'we don't want this great discovery (testosterone) to be the subject of snickers or back-room talk,' and the advice that the drugs would be mailed to customers in plain paper, indicate that the circulars were to be read in the light of the prospective customers' sexual problems and that the customers

themselves, rather than physicians, could judge of the beneficial results within ten days of taking. All of the foregoing is to be considered in the light of appellees' extensive campaign of advertising to tell *every man* and *every woman* where they could buy the hormones at their favorite drugstores.

"'The words, "adequate directions for use," necessarily relate to some purpose which is to be served by the use, and that purpose must be consistent with the intent of the Act as a whole to protect the public health. For what purpose are drugs used? Obviously, as a remedy for some ailment of the body. It seems equally obvious that no drug can be said to contain in its labeling adequate directions for its use, unless every ailment of the body for which it is, through any means, held out to the public as an efficacious remedy be listed in the labeling * * *.' United States v. Various Quantities of 'Instant Alberty Food,' 83 F. Supp. 882 (D. C. D. C.); see Alberty Food Products Co. v. United States, 185 F. 2d 321 (C. A. 9); Colgrove, et al. v. United States, 176 F. 2d 614 (C. A. 9). The proofs are convincing that appellees are implicitly holding out to the public, and selling, the drugs in question for some use other than that set forth in the directions for use.

"Moreover, the evidence discloses that in an investigation conducted in California, where the drugs were sold by appellees, by the Food and Drug Administration, subsequent to the criminal convictions, out of nineteen purchasers of the drug in question, selected at random, only one was deterred from taking testosterone as a result of reading the label. Another purchaser happened to read a newspaper article warning of the dangers and decided not to use it; and a third purchaser considered that its use was causing tension around his heart and nervousness, and stopped taking it. The remaining sixteen took the drug without consulting a physician. This evidence rather clearly shows that there were not adequate directions for use, or adequate warnings to the public. For, the label[7] would not necessarily indicate to a prospective user anything more than that the purpose of consulting a physician was to determine whether the drug would be beneficial to him; and there is no indication in the warning label that a physician should be consulted to determine whether the drug was dangerous for him. The evidence disclosed that the reference to a physician in the labeling of the drug had little effect upon the public, and indicates how unlikely it was that a mail order, or 'over the counter,' purchaser of this dangerous drug would take it to a physician and ask whether he should use it.

"In the submission of their arguments, appellees leave the crucial questions in the case unanswered. If it is dangerous to take a drug except under a physician's supervision, and if the distributors of such a drug do not want persons to take it except under a physician's supervision, what objection can they have to selling it only upon the prescription of a physician? And if they do not want persons to take it except under a physician's supervision, why do they exploit and promote such a drug, so restricted in its usefulness, by indiscriminate, widespread appeal directly to the public, offering customers sales in bargain lots when, as a result of such methods, it is most unlikely that physicians will be consulted by such customers? The failure and inability to give any adequate answers to these questions have transcendent significance. For the reasons we have indicated, in addition to those heretofore discussed, it is our conclusion that appellees' drugs did not bear adequate directions for use; that, further, they did not bear the adequate warnings required by the statute; and that such drugs must, therefore, be deemed to be misbranded.

"While appellees were not distributing female hormones when the complaints were filed in these cases, they had previously been engaged in such merchandising transactions. Circulars issued by appellee, Hudson Products Co., since the criminal cases, indicated a likelihood that they would do so again; and, although not a part of the record, the government, in its brief, set forth that newspaper advertisements by appellee, Vita Pharmacals, Inc., of female hormones had appeared since the filing of the complaints in the instant cases; and the facts so alleged are not denied. The government, in its complaints, asked for injunctions against the distribution of the female hormones in question. Under the above circumstances, we are of the view that such injunctions may properly issue.

"In consideration of the foregoing, the judgment of the district court is

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[7] See footnote 6.

reversed, and the case remanded, with directions to issue permanent injunctions as prayed for by the government in its complaints."

On June 26, 1951, the Government filed a motion with the United States Court of Appeals for the Ninth Circuit for issuance of its mandate in the cases to the District Court, with instructions to issue temporary restraining orders without notice pending the issuance of a permanent injunction. A motion was filed also on behalf of the defendants, requesting a stay of the mandate. The following opinion was handed down by the appellate court in denial of both motions:

FOR THE COURT: "The United States has moved this court for an order directing that mandate be issued forthwith. The motion is based upon the court's finding in its opinion of June 18, 1951, 'that the drugs in question are inherently dangerous; that they are not safe and efficacious for use except under the supervision of a physician; and that they are not suitable for self-medication, since a layman cannot know when they should be used and when they should not be used.'

"In support of the motion, the United States has produced two circulars mailed by the appellee Vita Pharmacals, one dated May, 1951, and the other circulated after this court's decision. The first circular advises of the pendency of the appeal in this court of this case and of the possibility of an adverse decision in which event appellee will be forced to discontinue the sale of its hormone products immediately. The circular therefore suggests that the recipient order an ample supply as an appeal to the United States Supreme Court would take at least a year to be heard. The exhortation is 'Don't delay. Order today . . As this may be your last opportunity to buy our products.' The second circular is headed in large type: 'QUITTING BUSINESS—IMPORTANT NOTICE! LAST TWO WEEKS TO PURCHASE OUR VITA HORMONE PRODUCTS.' The circular announces the decision of this court and suggests that in view of the impending cessation of the sales, the recipient stock up with an ample supply. There is no showing as to the extent to which such communications had been circulated, but the first circular recites: 'This is an answer to thousands of letters we have received from our interested customers with reference to the outcome of our FEDERAL LITIGATION.'

"The Government's motion proceeds upon the theory that until this court's mandate is returned to the District Court that court is without power to issue an injunction, and that unless the issuance of the mandate be expedited, the appellees will flood the country with products which this court has now determined to be highly dangerous to the public under the conditions which attended their distribution heretofore.

"We are of the opinion that upon the showing made by the United States, it is entitled to immediate relief by way of a temporary injunction which, as this court's opinion discloses, is required in the interest of the protection of the public. We think that the wording of the circulars mentioned would be well calculated to induce the appellees' customers to stock up with supplies of these drugs not merely for a few months but for years to come in view of the customers' reasonable apprehension that this court's judgment might ultimately be affirmed and that there might not be another opportunity to buy so freely. However, we do not find it desirable that the mandate issue forthwith in view of the fact that the time for filing petition for rehearing has not expired. We should hesitate to issue a mandate knowing that at the time it is issued we might have to recall it in order to entertain any petition for rehearing.

"Under Rule 62, Rules of Civil Procedure, two modes of procedure are open to the appellant neither of which involves a shortening of the time for the issuance of the mandate. Subdivision (c) of Rule 62[8] authorizes the district court to grant an injunction during the pendency of an appeal. Subdivision

[8] "(c) Injunction pending appeal. When an appeal is taken from an interlocutory or final judgment, granting, dissolving, or denying an injunction, the court in its discretion may suspend, modify, restore, or grant an injunction during the pendency of the appeal upon such terms as to bond or otherwise as it considers proper for the security of the rights of the adverse party. If the judgment appealed from is rendered by a district court of three judges specially constituted pursuant to a statute of the United States, no such order shall be made except (1) by such court sitting in open court or (2) by the assent of all the judges of such court evidenced by their signatures to the order."

(g)[9] of the same Rule recognizes the power of this court to grant an injunction during the pendency of the appeal here.

"The motion of the United States is not, in terms, an application for an injunction by this court, and it should not be entertained as such a motion not only because it does not seek such relief but also because this court is not as well equipped as is the district court to enforce an injunction of the type here sought.[10] Because the United States may obtain an injunction pending the time until mandate shall have reached the district court upon application to that court under Rule 62 (c), we deny the motion that mandate be issued forthwith.

"It is of course generally the rule that when an appeal is perfected the district court loses jurisdiction to take further action in the cause, but subdivision (c) of Rule 62 is an exception to that general rule and a recognition of the long established right of the trial court, after an appeal, to make orders appropriate to preserve the *status quo* while the case is pending in the appellate court. Newton v. Consolidated Gas Co., 258 U. S. 165, 177.[11]

"Under old equity rule 74, 226 U. S. 670, the trial judge was permitted to make such an order when he allowed the appeal, 'at the time of such allowance.' Subdivision (c) of Rule 62, omits reference to any specific time when the district court may grant such an injunction, and we think that under common principles of construction, this authority of the district court must now be held to continue throughout the period when the appeal is pending. Such injunction must be supported by appropriate showing and findings. Mayflower Industries v. Thor Corporation, 182 F. 2d 800.

"Accordingly the motion that mandate be issued forthwith is denied without prejudice to the right of appellant hereafter to make application to this court for such further order as it may hereafter be advised to seek.

"For the reasons which we have herein expressed, appellees' motion for stay of mandate is denied."

In accordance with the foregoing opinion, a motion for a temporary restraining order was filed on July 5, 1951, with the United States District Court for the Southern District of California. On the same date, the motion was granted and a temporary restraining order issued temporarily enjoining the defendants in each of the consolidated cases from commission of the acts complained of.

On July 31, 1951, following receipt of the mandate of the appellate court, findings of fact and conclusions of law were filed in each case in accordance with the appellate court's opinion of June 18, 1951.

With respect to the case against the El-O-Pathic Pharmacy, a corporation, it was pointed out that the corporation was dissolved on September 7, 1949, and was no longer in existence; and, accordingly, the complaint for injunction was dismissed as to this defendant. On the same day, an order was entered permanently enjoining Martin A. Clemens and Vita Pharmacals, Inc., from violating Sections 301 (a) and 301 (k), by distributing *male or female sex hormones* misbranded under Sections 502 (a), 502 (f) (1), 502 (f) (2), or 502 (j).

The nature of the injunction entered in the case against the Hudson Products Co., et al., is set forth in notices of judgment on drugs and devices, No. 3553.

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[9] "(g) Power of Appellate Court Not Limited. The provisions in this rule do not limit any power of an appellate court or of a judge or justice thereof to stay proceedings during the pendency of an appeal or to suspend, modify, restore, or grant an injunction during the pendency of an appeal or to make any order appropriate to preserve the *status quo* or the effectiveness of the judgment subsequently to be entered."

[10] Cumberland Tel. Co. v. Pub. Serv. Comm., 260 U. S. 212, was a case in which the Supreme Court recognized its power to grant a temporary injunction but considered it more appropriate to refer the application to the trial court.

[11] The *status quo* which the action was brought to preserve, was the protection of the public against the sale of certain misbranded drugs. The decision of this court is to the effect that such relief should have been granted.